AMENDMENTS TO THE DRAWINGS

Please replace the drawings with the Replacement Sheets provided herewith.

In addition, two "Annotated Sheets" are provided for two drawings that are canceled.

REMARKS

The Specification is amended to be in compliance with 35 U.S.C. § 112, first paragraph, which requires that the specification be written in "full, clear, concise and exact terms." Drawing "Replacement Sheets" are submitted herewith, wherein Figures 2 and 4 are canceled. Former Figures 3, 5 and 6 are now Figures 2, 3 and 4, respectively. In compliance with MPEP 608.02(t), the Applicants also submit "Annotated Sheets" for former Figures 2 and 4, which indicate that these two figures are canceled. Support for amendment to Claim 1 is found in the Specification as filed at page 5, lines 15-19; page 6, lines 18-23; page 98 (Example 19); and in former Figure 6, now Figure 4. Claims 24-33 are canceled without prejudice. No new matter has been added herewith. The following addresses the substance of the Office Action.

Objections to the Specification

(i) Figure 2 and Examples 12, 13 and 15

The Examiner noted that there is no description as to which particular T cell population or assay conditions correspond to the bars of the graphs in Figure 2. The results shown in Figure 2 relate to Example 12 and/or 13. As the results of Examples 12 and 13 are already described in each example, the Applicants have deleted Figure 2 and the accompanying description on page 8.

The Examiner also objected to the reference to Figures xb, 2C and 3C, which are not present in the specification. The Applicants have deleted references to these Figures in Examples 12 and 13 on page 95 of the Specification as filed. In addition, Applicants have deleted the reference to Figure 2 from Example 15.

(ii) Figure 4 & Example 17

The Examiner also stated that it is difficult to interpret the data displayed in Figure 4. In particular, the Examiner stated that the description on page 8 do not provide enough information to determine which T-cell population or assay conditions correspond to each dot plot. The Examiner also noted that the description of Figure 4 in Example 17 states that PMA/ionomycin was used to activate the cells (see page 98, lines 3A), while the description of Figure 4 on page 8 of the specification states that immobilized anti-CD3/CD28 antibodies was the activating agent. Since the description in Example 17 describes the results obtained, the Applicants have deleted Figure 4 and the references to Figure 4 on pages 8 and 98 of the Specification.

(iii) Example 19 & Figure 6

The Examiner noted that the heading of Example 19 stated that CDRF-35$^+$ CD45RO$^+$ CXCR3$^+$ T cells are depleted from peripheral blood of patients with psoriasis, but that CD45RO depletion is not mentioned in the example or in the description of Figure 6 on page 9. The Applicants have deleted the reference to CD45RO from the heading for Example 19.

The Examiner also objected to the phrase "Using the above-identified methods ..." in Example 19 on page 98, when referring to the isolation of PBMCs from peripheral blood from normal donors and patients with psoriasis. In response, the Applicants have amended this phrase to read: "Using the same method as disclosed in Example 2..."

(iv) Example 20

The Examiner noted some misspellings in Example 20. The Applicants have made the following amendments:

"wee" is amended to read "were",

"Breast" is amended to read "Breast cancer",

"thrombocyopenia" is amended to read "thrombocytopenia",

"throiditis" is amended to read "thyroiditis", and

"duseases" is amended to read "diseases".

The Examiner also stated that "Grave disease" is misspelled. However, Example 20 uses the term "Graves disease." The Applicants have added an apostrophe to the end of the word to yield "Graves' disease."

(v) Additional clarity notes

In addition to the Examiner's clarity objections, the Applicants have made the following amendments:

At page 6, line 14: the repeat of the phrase "and subjecting said CD4+ T cells" is deleted;

At page 12, line 25 and page 13, line 15: the term "CDCR3$^+$" is amended to read "CXCR3$^+$";

At Example 1: the term "Directly" is deleted from the first line, start of the second sentence;

At Example 2: the second paragraph is deleted;

At Example 4: the spelling of "Leucocyte" in the title is corrected and a space is inserted between "cells" and "were" at page 89, line 29;

At Example 6, line 7: the word "recommendations" is deleted before Pharmingen;

At Example 13, the spelling of the word "Example" is corrected;

At Example 22: the spelling of "psoriasis" is corrected on the first line.

Enablement

Claims 21-24, 29, 31, 32 and 37 were rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement. In particular, the Examiner stated that the term "immunological potential" was not defined and that the Specification fails to provide evidence that an overabundance or a deficiency of the various recited subsets of T cells leads to a change in the "immunogenic potential" of a subject.

Claim 21 is amended to remove recitation of a method for assessing the immunological potential of a subject. Instead, Claim 21 now recites a method for diagnosing psoriasis in a subject. Support for the amendments finds support in the Specification as filed, for example at Examples 19-22. In particular, Example 19 and Figure 4 (formerly Figure 6) show that the $CD4^{+}CMRF\text{-}35^{++}CXCR3^{+}$ population of cells is significantly reduced in peripheral blood mononuclear cells taken from patients with psoriasis compared to normal control patients. Thus, the Specification is enabling for the claimed methods of determining whether a subject has or is at risk of developing psoriasis.

The Examiner indicated that the CMRF-35 antibody used to distinguish between the various subsets of $CD4^{+}$ T cells was unknown and that the CMRF-35 antibody used must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. However, this antibody is commercially available in both polyclonal and monoclonal form. For example, the polyclonal antibodies to CMRF35 are available from Antibodies-online.com, and monoclonal antibodies to CMRF35 are commercially available from USBiological. Technical data sheets from each of these companies evidencing the availability of the antibodies to the public are enclosed.

The presently amended claims are specifically directed to determining an amount of T-cells in a sample that express CD4, CMRF-35 and CXCR3 cell surface markers. The antibodies for CD4 and CSC3 cell surface markers are also readily available to the public. For example, an FITC-labeled CXCR3 antibody obtained from R&D Systems (UK) can be used to determine the amount of T-cells that express the CXCR3 cell surface marker. The technical data sheet for this antibody is also enclosed. In light of the many scientific uses of the CD4 marker, antibodies specific for the CD4 cell surface marker are also exceedingly well known and are commercially

available from a large number of sources. Thus, one of ordinary skill in the art would be able to obtain all of the antibodies needed practice the claimed invention. Accordingly, the scope of the claims is fully enabled by the specification as filed.

Written Description

Claims 21-24, 29, 31, 32 and 37 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner indicated that the specification does not provide adequate support for the genus of cell surface discrimination means to detect and distinguish CMRF-35^{++} from CMR-35^{+} and CMRF-35^{-}. However, the present claims specifically relate to determining the amount of T-cells in a sample that express the surface proteins CD4, CMRF-35 and CXCR3. This is done using the CMRF-35 monoclonal antibody described by Daish et al. (*supra*), the FITC-labeled CXCR3 antibody by R&D Systems (UK) and antibodies that are specific for the CD4 surface marker. Thus, the Specification provides written support for the claims.

The Examiner also stated that the Applicants have not disclosed what particular epitope shared between various types of CMRF-35 (e.g., CMRF-35A, CMRF-35A2, CMRF-35A3, CMRF-35A4, CMRF-35A6 and CMRF-35H) is recognized by the particular CMRF-35 antibody. However, the presently amended claims are limited to the detection of T cells that express the CD4, CMRF-35 and CXCR3 surface markers. As indicated at page 2, lines 30-31 of the Specification as filed, both CMRF-35A and CMRF-35H molecules are identified by the CMRF-35 monoclonal antibody described by Daish et al (*supra*). Referring to page 4, lines 14-17, the CMRF-35A and H molecules are identified by the CMRF-35 monoclonal antibody, which binds to a functional epitope expressed on most human leukocyte populations. To practice the presently claimed method, it is not relevant which epitope is detected by the antibody. Rather, the method quantifies the amount of T cells that express the CMRF-35 surface marker. Accordingly, the claimed methods are in compliance with 35 U.S.C. § 112, first paragraph and the Applicants respectfully request that the rejection be withdrawn.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather,

any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

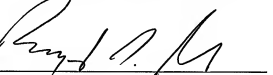
In view of Applicants' amendments to the Specification and the Claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: June 23, 2009

By: 

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